LOCATION, LOCATION, LOCATION: THE IMPACT OF ONE'S NEIGHBORHOOD ON OUTCOMES FOLLOWING PROCTECTOMY FOR RECTAL CANCER

A Master's Thesis Presented

By

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Abstract

Purpose: The area deprivation index (ADI) is a comprehensive assessment of the social determinants of health. The higher the composite ADI score, the more underserved the area. This study examined the impact of a patient's ADI score on surgical, pathologic, and survival outcomes following proctectomy for rectal cancer.

Methods: Data from a single tertiary care medical center's targeted National Surgical Quality Improvement Program (NSQIP) were used to identify all patients undergoing proctectomy for rectal cancer between January 2014 – December 2022. A state ADI (ranking 1-10) was assigned to each patient using their residential address. Patients were categorized into Low (1-4), Moderate (5-6), High (7-8), and Very High (9-10) ADI groups.

Results: Two-hundred and four patients who underwent proctectomy for rectal cancer were included. There were no significant between group differences in patient's post-operative outcomes including 30-day morbidity and hospital readmissions. As well as pathologic outcomes, including completeness of mesorectal excision and rate of positive margins. A Cox multivariable adjusted regression model showed those in the Very High group had a higher risk of dying at 5 years than the Low ADI group. Patients in the Very High and High ADI groups were significantly more likely to be discharged somewhere other than home after their surgery than those in the Low ADI group, (13% vs. 0%). The median time from diagnosis to initiating treatment or surgery showed those in the Very High and High ADI groups took longer to obtain treatment.

Conclusion: A patient's ADI has an impact on their overall survival following proctectomy for rectal cancer and influences their time to receiving treatment and their postoperative disposition. Future studies with larger patient cohorts are needed to more clearly define the role of ADI in predicting patient outcomes following proctectomy for rectal cancer.

Introduction:

Colorectal cancer remains the fourth most commonly diagnosed cancer in the United States and the second most common cause of cancer related deaths.[1] In 2024, it is estimated that more than 46,000 new cases of rectal cancer alone will be diagnosed in the U.S. with these individuals undergoing complicated and extensive treatment for their disease with variable outcomes.[2] There are many disparities seen in the outcomes associated with rectal cancer, whether it be the time from diagnosis to the receipt of treatment, how well patient's fare during treatment, and post-operative outcomes including functional status and long-term survival. African Americans, Indigenous individuals, people of color (or BIPOC), and those from lower socioeconomic strata are more likely to experience worse survival and functional outcomes after treatment for rectal cancer than their Caucasian or more affluent counterparts. [3-6,8,22-23]

The reasons for disparities in these outcomes include factors such as access to care/screening, underrepresentation in clinical trials, health literacy, lack of insurance coverage, and patient's ability to seek screening as well as treatment.[7-9, 24-25] However, despite this knowledge, we still lack a quantitative measure that will indicate when a patient is at higher risk for worse surgical, survival, and quality of life outcomes in those with rectal cancer.

The area deprivation index (ADI) is a comprehensive assessment of the social determinants of health. The ADI was initially developed by the US Health Resources and Services Administration.[10-11] and was further refined at the Census block group neighborhood level.[11] Each census block group area is analyzed based on 17 variables and reported as a composite score.[12] The higher the ADI the more underserved the area. A State level ADI is measured in deciles, with a score of 10 representing the most underserved.[11-12]

The ADI has been used to examine differences in mortality and other outcomes in patients with breast cancer and COVID-19 as well as to predict surgical morbidity and associated costs in patients undergoing general surgery.[13-15] In these studies, the ADI has proven to be a good measure for determining risk commonly associated with socioeconomic factors that go beyond the patient's or their household's income status. The objective of this retrospective cohort study is to investigate whether a patient's ADI score is associated with long-term survival and post-operative outcomes in patients who underwent proctectomy for primary rectal malignancies at a single tertiary care medical center.

Materials and Methods:

Data Source:

We carried out a retrospective cohort study in which we used information from a single institution's National Surgical Quality Improvement Program (NSQIP) database and a departmental specific database of patients undergoing transanal total mesorectal excision (taTME). ADI scores were assigned to patients utilizing the Neighborhood Atlas mapping feature from the most recent version of this database in 2021.[11]

Study Population:

Our study population included all adult patients (≥18 years-old) who underwent a proctectomy for rectal cancer between January 2014 and December 2022 who were in the institution's NSQIP and taTME databases. This time frame was chosen to allow for patients to be followed for at least one year after undergoing their surgery and include patients starting from

the first year the databases were maintained. The proctectomies were completed by either minimally invasive (laparoscopic or robotic), open, or transanal surgical approaches and all were performed by a general or colorectal surgeon at the University of Massachusetts Memorial Medical Center.

Study Design:

The final study cohort consisted of 204 patients who met our inclusion criteria. The State-level ADI was utilized (ranking from 1-10) and assigned to each patient using their address at the time of their surgery. For purposes of analysis, patients were categorized into Low ADI (1-4), Moderate ADI (5-6), High ADI (7-8), and Very High ADI (9-10) groups.[14] Variables such as race, primary payor status, and current tobacco use were derived from the patient's self-reported status as noted in their electronic medical record (EMR). Other variables including American Anesthesiology Association (ASA) score, functional health status, body mass index, and other diagnoses were derived from information available in patient's EMRs, including operative and clinical reports. Deidentified data for the variables of interest were extracted from the respective databases.

Primary Study Outcome

The primary study outcome was patient's long-term survival after undergoing proctectomy for rectal cancer. Patient's EMRs were reviewed to identify patient's long-term survival status and patients were followed through the end of calendar year 2023. Survival time was calculated using the date of the patient's surgery until the date of last contact or date of death listed in their EMR.

Secondary Study Outcomes

Our secondary study outcomes included the time from the diagnosis of rectal cancer to treatment and completeness of pathologic resection. Time to treatment was defined as the time, in days, between a patient's biopsy confirmed diagnosis of rectal cancer until when they started receiving their first chemotherapy and/or radiation treatment or underwent surgery. The date of the patient's last cancer related clinical contact or appointment was used to assess median follow up time. Pathologic data, including American Joint Committee on Cancer (AJCC) Stage based on tumor/node/metastasis (TNM) status, receipt of neoadjuvant and adjuvant therapy, distal and radial margin status, completeness of the mesorectal excision, and number of lymph nodes examined were taken directly from patient's pathology reports. This was used to determine the quality of surgical resection for each patient. Follow-up times were recorded from the date of surgery until the patient's last documented cancer-related follow-up appointment as noted in their chart. Other secondary outcomes included 30-day post-operative outcomes including hospital readmission, discharge destination, sepsis, and surgical site infections that may have developed during the 30-day period after the patient's initial surgery.

Statistical Analysis:

Demographic and clinical variables were described for the entire study cohort and then compared between patients according to the four state ADI scores. Between group differences in patient's baseline characteristics and post-operative/pathologic outcomes were examined using Student's t-test or analysis of variance for continuous variables and chi-square or Fisher's exact

test for categorical variables, where appropriate. Kaplan-Meier survival curves were created to examine differences in long-term survival between the respective ADI groups while accounting for losses to follow-up and date of last follow-up. Cox-regression models were used to examine the association between ADI and long-term survival by computing hazard ratios and their 95% confidence intervals, while controlling for age and AJCC stage.

Results:

Study Population Characteristics:

The final study cohort consisted of 204 patients who underwent surgery for rectal cancer between January 2014 and December 2022. The mean age of this study population was 59.9 (SD ± 12.6) years, two-thirds were men, and the majority of the study population identified as Caucasian (87.0%); only 3.4% identified as African American. When grouped according to the state ADI score, 78 patients were classified as Very High (38.2%), 60 as High (29.4%), 40 as Moderate (19.6%), and 26 as Low (12.7%).

Table 2 presents a summary of the socio-demographic and clinical characteristics of the four ADI groups. Patients in the High or Very High ADI groups had a higher body mass index, were more likely to have been previously diagnosed with diabetes, and to be a current smoker prior to their surgery compared with the Low ADI group. Patients with a high ADI score were more likely to be malnourished or were partially functional prior to their surgery. An ASA Class less than 3 was more often observed in the Low than in the Very High ADI group indicating lower overall pre-operative morbidity in these individuals. Patients in the Moderate ADI group had the highest proportion of patients who were immunosuppressed compared with the other ADI groups.

Outcomes According to ADI

Long-Term Survival

Two-hundred and one of the 204 patients included in this study had further follow-up information available . The median follow-up time of these 201 patients was 42 months (IQR 19,66) and a median time until death of 31 months (IQR 15, 43) was observed for the 54 patients who died over the course of our extended follow-up. In evaluating survival at 1-year post-op, patients in the Moderate ADI group experienced the highest survival while those in the High ADI group had the lowest. In contrast, at year 2, the highest survival was observed in the Low ADI group and the lowest survival in the Very High ADI group; these differences continued to be observed until year 5 (Table 6). Similar trends were observed in the Kaplan Meier curve as shown in Figure 1.

After controlling for age and AJCC stage, patients in the Very High ADI group were more likely to have died over the course of our extended follow-up compared with the Low ADI group. (Table 3).

Clinical Outcomes and Pathologic Variables

The median time from the diagnosis of rectal cancer to initiating treatment or surgery was longest in the Very High and High ADI groups (Table 4). Patients in the Very High and Moderate ADI groups were more likely to receive neoadjuvant therapy than those in the Low and High groups. In contrast, patients in the High and Very High ADI groups had lower rates of adjuvant

therapy than those in the Moderate and Low ADI groups. Complete mesorectal excision was achieved in 85% of patients in the Low, Moderate and High ADI groups, but in only 79% of patients in the Very High ADI group. However, as seen in Table 4, this group did have a larger median tumor size seen on pathology at 3.2cm than the other three groups whose median tumor size ranged from 2.3-2.5cm.

Post-operatively, patients in the Very High and High ADI groups were significantly more likely to be discharged somewhere other than home after their surgery (Table 5). The Very High ADI group was more likely to be discharged to a skilled nursing facility while the High ADI group was more likely to be discharged to a rehabilitation facility.

In examining between group differences in post-operative morbidity during the first 30-days of surgery, the High and Very High ADI group had higher rates of sepsis, surgical site infections, and hospital readmissions than the Low and Moderate ADI groups (Table 5).

Discussion:

The results of this retrospective cohort study suggest that a patient's ADI score is associated with their likelihood of long-term survival in patients who underwent a proctectomy for rectal cancer. Those residing in areas assigned with a Very High ADI were less likely to be alive at 5 years than those with a Low ADI score. Higher ADI was associated with a longer time gap between the time of diagnosis until treatment as well as lower likelihood of receiving adjuvant chemotherapy. Patients with higher ADI scores also being more likely to be discharged to a facility other than their home after surgery.

ADI and long-term survival in patients undergoing proctectomy for Rectal Cancer:

We found that ADI was associated with worse outcomes in those undergoing proctectomy for primary rectal malignancies, particularly with regards to long-term survival. These findings were similar to results seen in previous studies that have examined the effects of ADI on survival among patients with colorectal cancer.[21] One retrospective study of patients with pathologically confirmed colorectal cancer between 2007 and 2015 extracted from the SEER database showed a significant association between a patient's ADI score and their survival probability. This study examined 266,620 patients with 131,980 classified as low ADI patients and 127,719 classified as high ADI patients. The high ADI group had a significant association with the male sex, older age, black race and higher likelihood of not having received treatment. While the low ADI group was more likely to be married and insured than the high ADI group. Similar to our results, this study showed that patients in the high ADI group scored neighborhoods fared worse for both overall and cancer-related survival than those in the Low ADI group seen in both their Kaplan Meier curves as well as the unadjusted and adjusted multivariate analyses.

The prior study of colorectal cancer patients from the SEER database also examined the impact that ADI had on a patient's likelihood to receive any "anti-cancer" therapy, including chemotherapy, radiation, or combination therapy both in the neoadjuvant and adjuvant setting. They found that those in the High ADI group were less likely to receive any "anti-cancer" therapy during their disease course which had an adverse impact on their survival compared with the Low ADI group. [21] Our study showed similar findings in that the High and Very High

ADI groups were less likely to have received adjuvant chemotherapy compared to the Low and Moderate ADI groups.

Important prognostic variables, such as the length of time from diagnosis until treatment, and the timing and extent of patient follow up, have been shown to be significantly impacted by individual-level social barriers, including median household income and insurance status that may affect one's ability to seek, establish, or continue care.[25] There are a paucity of studies, however, that have examined the role that neighborhood-level factors, such as the ADI score, may exert on these impactful outcomes. In the present study we were able to show that those in the Low and Moderate ADI groups had a shorter length of time from diagnosis until initiating treatment than those in the High and Very High groups. This may reflect the large number of sociodemographic variables ADI encompasses that play a role in patient's barriers to care, but it could also point to ADI potentially acting as a good prognostic surrogate to identify those at higher risk for adverse outcomes.

We also found that ADI was significantly associated with where patients were discharged to from the hospital after undergoing surgery, with those in the higher ADI group more likely to be discharged to a non-home destination. Previous studies have shown that factors such as post-operative complications, advanced age, functional dependence status, and ASA class ≥3 were associated with patients not being discharged to their homes.[17-18] However, when patients were categorized by their respective state ADI scores, we found no statistically significant difference in patient demographics/comorbidities outside of their primary payor insurance status. This may suggest that the neighborhood-level sociodemographic factors in the ADI score may play an important role in determining patients post-operative disposition.

Study strengths and limitations:

The strengths of our study include that our data were derived from a comprehensive database which allowed us access to many clinically important variables for analysis. The use of a state ADI database also allowed for a more comprehensive assessment of between neighborhood differences as it compares them within the context of their own state and revealed disparities in patient characteristics in these areas that may be lost on a larger national scale. Our study also helped to add further context for the use of ADI among patients with rectal cancer since there is a paucity of data in this area. We acknowledge that this study is limited by its retrospective nature and small sample size. This study also used data from a single health system from a single region of the country which may have limited the generalizability of our study findings. Inasmuch, further investigation is warranted using data from a larger patient cohort from a broader geographic region to more comprehensively understand the role ADI may play in outcomes for this patient population.

Conclusions:

A patient's ADI has an impact on their overall survival following proctectomy for rectal cancer. ADI also appears to play a role in a patient's time to receiving treatment following their diagnosis of rectal cancer and influences their postoperative disposition. Future studies with larger patient cohorts will help to more clearly define the role of ADI in predicting patient outcomes and potentially be used as a surrogate to improve both short and long-term outcomes in patients with rectal cancer.

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Tables/Graphs:

Table 1. Factors used to determine the Area Deprivation Index (ADI)
Percent of population aged ≥25 years with <9 years of education
Percent of population aged ≥25 years with a high school diploma
Percent of employed persons ≥16 years of age in white collar occupations
Median family income
Income disparity
Median home value
Median gross rent
Median monthly mortgage
Percent owner-occupied housing units (home ownership rate)
Percent of civilian labor force ≥16 years of age that is unemployed
Percent of families below the poverty level
Percent of population below 150% of the poverty threshold
Percent of single-parent households with children <18 years of age
Percent of households without a motor vehicle
Percent of households without a telephone
Percent of occupied housing units without complete plumbing
Percent of households with more than one person per room

Table 2. Study population characteristics according to State ADI score

Characteristic	**Low ADI (1-4) (n=26)**	**Moderate ADI (5-6) (n=40)**	**High ADI (7-8) (n=60)**	**Very High (9-10) (n=78)**	**p-value**
Age (years, mean ± SD)	59.8 ± 10.9	56.5 ± 15.1	60.0 ± 12.3	61.5 ± 11.8	0.24
Sex					0.52
Male, n (%)	17 (65.4)	23 (57.5)	43 (71.7)	53 (67.9)	
Race, n (%)					0.36
Asian	2 (7.7)	0 (0)	0 (0)	2 (2.6)	
Black or African American	0 (0)	1 (2.5)	2 (3.3)	4 (5.1)	
Hispanic or Latino	0 (0)	1 (2.5)	2 (3.3)	6 (7.7)	
Other	1 (3.9)	0 (0)	1 (1.7)	0 (0)	
Unknown/not reported	0 (0)	0 (0)	1 (1.7)	3 (3.9)	
White	23 (88)	38 (95)	54 (90)	63 (81)	

Primary Payor Status (Insurance)					0.03
Medicaid	0 (0)	4 (10.0)	7 (11.7)	14 (17.9)	
Medicare	3 (11.5)	5 (12.5)	17 (28.3)	20 (25.6)	
Private insurance	16 (61.5)	15 (37.5)	20 (33.3)	20 (25.6)	
Malnourished	0 (0)	1 (2.5)	3 (5.0)	0 (0)	0.14
Functional Health Status					0.60
Independent	26 (100)	39 (97.5)	56 (93.3)	73 (93.5)	
Partially Dependent	0 (0)	1 (2.5)	4 (6.7)	5 (6.4)	
Totally Dependent					
ASA Class, n (%)					0.13
I	0 (0)	1 (2.5)	1 (1.7)	1 (1.3)	
II	19 (73.1)	20 (50.0)	29 (48.3)	30 (38.5)	
III	7 (26.9)	18 (45.0)	28 (46.7)	46 (59.0)	
IV	0 (0)	1 (2.5)	2 (3.3)	1 (1.3)	
Current tobacco use/smoker	5 (19.2)	6 (15.0)	13 (21.7)	26 (33.3)	0.12
Body mass index, mean ± SD	26.9 ± 4.3	27.7 ± 6.1	29.5 ± 5.8	28.6 ± 6.3	0.22
Diabetes mellitus					0.21
Insulin	0 (0)	0 (0)	1 (1.7)	2 (2.6)	
Non-insulin	2 (7.7)	3 (7.5)	2 (20.4)	16 (20.5)	
History of COPD	0 (0)	1 (2.5)	2 (3.3)	2 (2.6)	0.08

Figure 1. Kaplan-Meier survival curves according to State ADI Score (n=201)

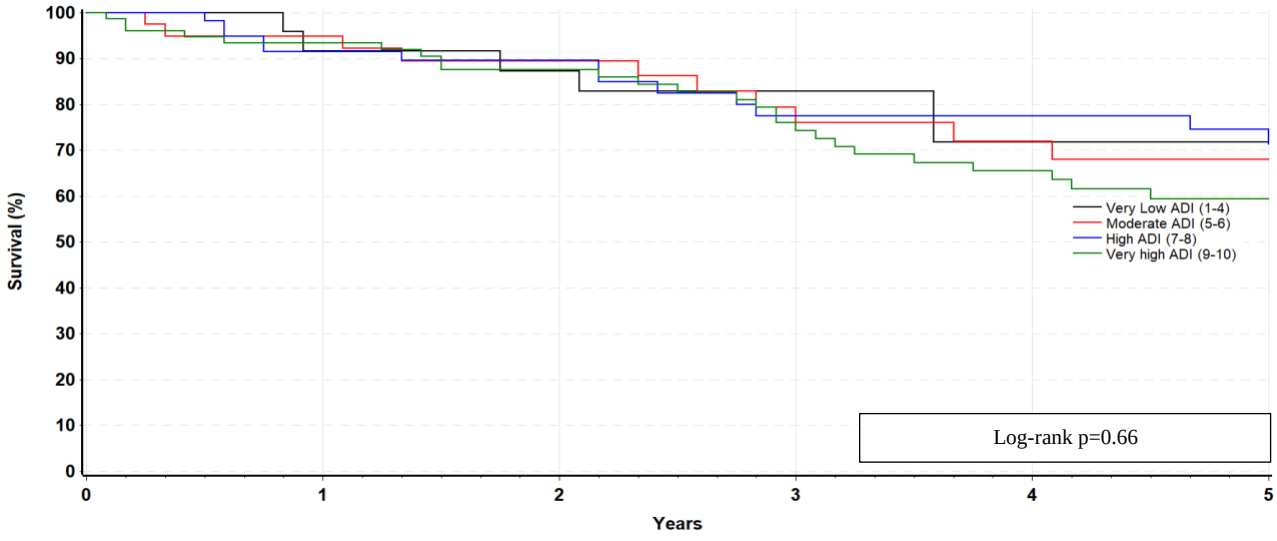

Table 3. Crude and multivariable adjusted Cox regression model predicting overall survival according to State ADI score		
	Crude Hazard Ratio (HR) [95% CI]	Adjusted HR* [95% CI]
State ADI (versus 1-4)	1 [Reference]	1 [Reference]
Moderate state ADI (5-6)	1.15 [0.42, 3.16]	1.21 [0.44, 3.32]
High state ADI (7-8)	1.02 [0.39, 2.68]	0.98 [0.37, 2.58]
Very high state ADI (9-10)	1.47 [0.60, 3.59]	1.37 [0.56, 3.35]
*controlling for age and pathologic AJCC Cancer Stage		

Table 4. Pathologic outcomes According to State ADI score

	Low ADI (1-4) (n=26)	**Moderate ADI (5-6) (n=40)**	**High ADI (7-8) (n=60)**	**Very High (9-10) (n=78)**	**p-value**
Pathologic AJCC Cancer Stage n, (%)					
Stage 0	5 (19.2)	5 (12.5)	10 (16.7)	6 (7.7)	
Stage 1	5 (19.2)	12 (30.0)	20 (33.3)	20 (25.6)	
Stage 2	6 (23.1)	7 (17.5)	18 (30.0)	22 (28.2)	
Stage 3	7 (26.9)	13 (50.0)	9 (15.0)	28 (35.9)	
Stage 4	2 (7.7)	2 (5.0)	2 (3.3)	2 (2.6)	
Proctectomy Margins-Radial Involvement	7 (26.9)	12 (30.0)	20 (33.3)	30 (38.5)	0.98
Proctectomy Clear Radial Margin Distance (cm)	1.0 (1.3)	0.8 (0.6)	0.7 (0.6)	0.8 (1.0)	0.66
Proctectomy Margins-Distal Involvement	7 (26.9)	14 (35.0)	20 (33.3)	31 (39.7)	0.94
Proctectomy Clear Distal Margin Distance (cm)	2.1 (2.2)	2.4 (1.6)	2.3 (1.7)	2.6 (2.0)	0.80
Received neoadjuvant therapy	20 (76.9)	33 (82.5)	46 (76.7)	64 (82.1)	0.82
Received adjuvant therapy	19 (73.1)	28 (70.0)	32 (53.5)	50 (64.5)	0.26
Median time until death, in months (IQR)	23 (11, 43)	33 (15, 47)	26 (9.0, 56)	35 (18, 44)	0.88
Median follow up time, in months (IQR)	43 (25, 70)	43 (24, 67)	35 (19, 65)	40 (18, 61)	0.82

Time from Diagnosis to Treatment, mean ± SD	39.6 ± 18.2	34.5 ± 16.8	47.0 ± 38.9	43.6 ± 25.7	0.17
Number of lymph nodes examined, median (IQR)	17 (12, 19)	15 (12, 20)	16 (12, 21)	15 (13, 19)	0.91
Tumor size, cm, median (IQR)	2.3 (0.7, 4.2)	2.4 (1.5, 4.2)	2.5 (1.5, 4.0)	3.2 (1.8, 5.0)	0.18
Completeness of mesorectum resection, n(%)					0.82
Complete (1)	22 (84.6)	34 (85.0)	50 (84.5)	61 (78.6)	
Nearly Complete (2)	3 (11.5)	5 (12.5)	5 (8.5)	13 (16.7)	
Incomplete (0)	1 (3.9)	1 (2.5)	4 (6.8)	3 (3.9)	
Circumferential resection margin involved <1mm, n%	5 (19.2)	3 (7.7)	6 (10.0)	6 (7.7)	0.40
Distal resection margin involved <1mm, n(%)	0 (0)	1 (2.5)	0 (0)	1 (1.3)	0.78
Free perforation of serosa, n (%)	3 (12)	4 (10)	2 (3.4)	4 (5.1)	0.34

Table 5. Thirty-day postoperative outcomes According to State ADI Score

	Low ADI (1-4) (n=26) n %	**Moderate ADI (5-6) (n=40) n %**	**High ADI (7-8) (n=60) n %**	**Very High (9-10) (n=78) N %**	**p-value**
Urinary tract infections	0 (0)	1 (2.5)	0 (0)	1 (1.3)	0.77
SSI (Surgical Site Infection)					
superficial incisional	1 (3.9)	1 (2.5)	6 (10.0)	8 (10.2)	0.43
deep/organ space SSI	2 (7.7)	1 (2.5)	7 (11.6)	5 (6.4)	0.40
Pneumonia	0 (0)	0 (0)	1 (1.7)	1 (1.3)	0.99
Sepsis	1 (3.9)	0 (0)	3 (5.0)	4 (5.1)	0.52
DVT	0 (0)	0 (0)	1 (1.7)	2 (2.6)	0.87
Post-operative bleeding	0 (0)	0 (0)	1 (1.7)	0 (0)	0.62
Required blood transfusion	0 (0)	1 (2.5)	3 (5.0)	6 (7.7)	0.51
Pulmonary Embolism	0 (0)	0 (0)	1 (1.7)	0 (0)	0.62
Additional surgeries - unplanned return to OR	1 (3.9)	0 (0)	2 (3.3)	3 (3.9)	0.67

Renal failure - requiring dialysis	0 (0)	0 (0)	1 (1.7)	0 (0)	0.62
Cardio-pulmonary complications (MI, cardiac arrest)	0 (0)	0 (0)	0 (0)	1 (1.3)	0.99
Post op Mortality/Death w/in 30 days of Surgery	0 (0)	0 (0)	2 (3.3)	0 (0)	0.27
Hospital re-admission w/in 30 days of surgery	4 (15.4)	4 (10.0)	9 (15.0)	16 (20.5)	0.52
Discharge Destination					**0.007**
Home	25 (100)	37 (92.5)	57 (95.0)	67 (85.9)	
Skilled Nursing/Care	0 (0)	3 (7.5)	0 (0)	10 (13)	
Rehab	0 (0)	0 (0)	3 (5)	0 (0)	

Table 6. Post-operative survival status according to ADI group

	Baseline	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Low ADI						
Number at risk	26	22	20	15	12	11
SE	0	0.056	0.069	0.078	0.099	0.099
Survival Rate	100%	92.0%	92.0%	82.9%	71.9%	71.9%
Moderate ADI						
Number at risk	39	36	29	23	18	10
SE	0	0.035	0.050	0.070	0.081	0.086
Survival Rate	100%	94.9%	89.5%	79.4%	72.0%	68.0%
High ADI						
Number at risk	59	53	39	30	27	23
SE	0	0.037	0.040	0.061	0.061	0.070
Survival Rate	100%	91.5%	89.6%	77.5%	77.5%	71.4%
Very High ADI						
Number at risk	77	68	55	45	36	21
SE	0	0.028	0.039	0.053	0.060	0.064
Survival Rate	100%	93.5%	87.5%	76.0%	65.6%	59.5%

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